

## REMARKS

### **I. Introduction**

This is in response to the Office Action dated January 11, 2005. Claims 1-5 are pending in this application. Applicants have canceled claims 6-21, without prejudice or disclaimer, reserving the right to file a divisional application on the non-elected inventions of claims 14-21. Applicants have amended claims 1-5. Support for these amendments can be found, for example, in Figs. 8-10, and at page 19, line 4 to page 21, line 8 of the specification. No new matter has been added.

For the reasons set forth below, Applicants respectfully submit that all pending claims are patentable over the cited prior art references.

### **II. Rejection Of Claims 1-13 Under 35 U.S.C. § 112, Second Paragraph**

Claims 1-13 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Claims 6-13 have been canceled thereby rendering the rejection as these claims moot.

With respect to the remaining claims, the Examiner asserts that it is unclear if a plurality of first binding sites are binding to a other single first binding site carried by an adjacent fine particle, and if the adjacent fine particle is the same as the protein fine particles. The Examiner further made a finding that it is unclear if the substitution of the condensed amino acids is a method step or if the second binding site comprises condensed amino acids, which are

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substituted for another entity on the protein fine particle. In response, Applicants have deleted the objected to language from claim 1-5 that gave rise to the rejection. Accordingly, it is respectfully requested that the rejection be reconsidered and withdrawn.

### **III. Rejection Of Claims 1-11 and 13 Under 35 U.S.C. § 103**

Claims 1-11 and 13 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Nagayama et al. ("Fabrication and Control of Two-Dimensional Crystalline Arrays of Protein Molecules," *Jpn. J. Appl. Phys.* 1995:34; 3947-3954) in view of Onda (U.S. Patent No. 6,107,084). Claims 6-11 and 13 have been canceled thereby rendering the rejection as these claims moot. Applicants respectfully request reconsideration of this rejection of the remaining claims 1-5 for the following reasons.

As described in the Background Art Section of the specification, it is difficult to transfer a two-dimensional crystal film onto a substrate using the conventional technique. More specifically, as illustrated in Fig. 12(d) of Applicants' drawings, Applicants have discovered that the film 28, comprising the amorphous film 26 and the two-dimensional crystal film 27 having the protein fine particles 45, is often damaged during the transfer thereof to the surface of the substrate 21. Applicants have further discovered that a two-dimensional crystal film having the protein fine particles arranged at a high density and in a highly accurate and regular manner cannot be obtained, because the directions of symmetric axes of the protein fine particles become random during the transfer process. This random directions of the protein fine particles cause the protein fine particles to form an aggregated structure.

In view of the foregoing problem and in accordance with one exemplary embodiment of the present invention, the amino acids of the apoferritin fine particle 15 located in the site R4 in the vicinity of the four times symmetric axis S4 are replaced with basic amino acid (i.e., an amino acid having positive charge). Specifically, glycine at position 149 and glutamine at position 151 are substituted with a basic amino acid. Accordingly, by utilizing the positive charge of the basic amino acids and the negative charge of the substrate, the apoferritin fine particles can be advantageously arranged at a high density and in a highly accurate and consistent manner.

By contrast, the cited prior art is completely silent as to the problems related to the arrangement of the protein fine particles, let alone the means by which to solve such problems as conceived by Applicants. In this regard, Nagayama et al. and Onda, at best, are merely cumulative to the admitted prior art described at pages 1-6 of Applicants' specification in that Nagayama and Onda are also subject to the same drawbacks as those of the conventional technique resulting from the random directions of symmetric axes of the protein fine particles and the aggregated structure resulting therefrom. It is respectfully submitted that the cited prior art neither recognizes nor considers such problems, nor suggests possible solutions.

Even assuming *arguendo* that the Examiner's proposed combination is proper, Nagayama et al. expressly disclose obtaining the 2D-crystals or 3D-crystals by utilizing apoferritin or mutant apoferritin (i.e., aspartic acid at position 84 and glutamine at position 86 are replaced by serine (Asp84Ser and Gln86Ser)) (see, Fig. 3 and Experimental Examples 3.1-3.3). Nagayama et al. further disclose that the carbon supporting film has to be previously hydrophilized by ion

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bombardment so as to enhance the adhesion of the protein arrays to the carbon supporting film (see, page 3949, right column, last 3 lines). However, with respect to the “4-fold symmetry,” Nagayama et al. are completely silent with regard to the elements of apoferritin at position 149 and position 151. They do not specifically disclose or suggest replacing the foregoing elements thereof with a basic amino acid. It is also important to note that Nagayama et al. do not discuss any arrangement of the apoferritin particles on a substrate through utilizing the *positive* charge of the basic amino acids and the *negative* charge of the substrate. Onda, on the other hand, only discloses the adsorption of a protein on a substrate by utilizing the charges of the substrate and the protein, but does not expressly disclose that the substrate is *negatively* charged. Therefore, Onda also does not cure the deficiencies of Nagayama et al.

Accordingly, for the reasons discussed above, the cited prior art is silent as to the features recited by amended claim 1, let alone in combination with the other features recited in their respective dependent claims. Indeed, the cited prior art is silent as to the associated structural benefits, identified only by Applicants, which can be rendered therefrom. Based on all the foregoing, it is submitted that claim 1 is patentable over Nagayama et al. and Onda, taken alone or in combination.

Accordingly, it is respectfully requested that the rejection of claims 1-5 over Nagayama et al. and Onda be reconsidered and withdrawn.

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**IV. Rejection Of Claim 12 Under 35 U.S.C. § 103**

Claim 12 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Nagayama et al. in view of Onda and Takada et al.. Claim 12 have been canceled thereby rendering the rejection as this claim moot.

**V. All Dependent Claims Are Allowable Because The Independent Claims From Which They Depend Are Allowable**

Under Federal Circuit guidelines, a dependent claim is nonobvious if the independent claim upon which it depends is allowable because all the limitations of the independent claim are contained in the dependent claims, *Hartness International Inc. v. Simplimatic Engineering Co.*, 819 F.2d at 1100, 1108 (Fed. Cir. 1987). Accordingly, as independent claim 1 is patentable for the reasons set forth above, it is respectfully submitted that all claims dependent thereon are also in condition for allowance.

**CONCLUSION**

Accordingly, it is urged that the application is in condition for allowance, an indication of which is respectfully solicited.

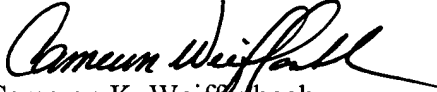
If there are any outstanding issues that might be resolved by an interview or an Examiner's amendment, the Examiner is requested to call Applicants' attorney at the telephone number shown below.

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To the extent necessary, a petition for an extension of time under 37 C.F.R. § 1.136 is hereby made. Please charge any shortage in fees due under 37 C.F.R. § 1.17 and in connection with the filing of this paper, including extension of time fees, to Deposit Account 500417 and please credit any excess fees to such deposit account.

Respectfully submitted,

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